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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,949	07/27/2006	M Bishr Omary	STAN-297	1285

77974 7590 05/05/2009

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EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
05/05/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/552,949	OMARY ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 29 April 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☒ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,3,6 and 7*.
   Claim(s) withdrawn from consideration: *5 and 8*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Carla Myers/
Primary Examiner, Art Unit 1634

Continuation of 3. NOTE: The amendment to the claims to recite that the change in genotype is relative to a wild-type sequence raises new issues that would also require further search and consideration under 35 USC 112 first paragraph (enablement) and 112, second paragraph. Note that the claims did not previously require comparing the genotype of the individual to any wildtype sequence of any gene (claim 1) or any wild-type sequence that encodes keratin K8 at position 340 (claims 3, 6 and 7). The amendment also appears to raise the issue of new matter. The response points to page 5, lines 1-18 and page 24, lines 8 to the end of page as providing support for this amendment. However, page 5 teaches only comparing the K8 sequence of an individual to a "normal" K8 nucleic acid sequence. The specification does not teach what constitutes a "normal" K8 nucleic acid sequence. Page 24 of the specification teaches that two offspring had a wild type K8 sequence as defined by the particular nucleotides encoding the amino acids at position 53, 61, 340, 433 and 465-468 and as specifically recited in Table 5. Table 5 defines the wild-type keratin K8 protein as having an arginine at position 340. The specification teaches a wild-type K8 protein that has an arginine at position 340, but this teaching does not provide support for the distinct concept of a wild-type K8 protein having any other amino acid at position 340. These teachings in the specification do not provide support for the broader concept encompassed by the claims of comparing the genotype of an individual with any wild-type sequence of any gene (claim 1) or with any wild-type sequence that encodes keratin K8 (claims 3, 6 and 7).

Continuation of 11. does NOT place the application in condition for allowance for the reasons of record in view of the non-entry of the after final amendment. It is noted that Applicant's arguments are directed to the claims as amended. However, since the after final amendment has not been entered, these arguments are not persuasive. To the extent that Applicants arguments are not directed to the claims as amended, these arguments have also been fully considered but are not persuasive. Regarding the enablement rejection, the response asserts that the claims meet the enablement requirement because the specification teaches how to determine the sequence of a polynucleotide and that this requires only routine experimentation. This argument is not persuasive because the claims are not directed to general methods for determining the nucleotide sequence of a K8 polynucleotide. Rather, the claims are directed to methods for determining a predisposition to any cryptogenic or non-cryptogenic liver disease. Applicants state that there may be some non-functional variants within the genus defined by the claims, but assert that Applicants are not required to establish that every species within a claimed genus will work. This argument has also been fully considered but is not persuasive. While Applicants are not required to establish that all species encompassed by the claims are operable, Applicants are required to establish the enablement of a representative number of species encompassed by the claims. In the present situation, Applicants have established an association only between the CGT to CAT mutation at the codon encoding position 340 of the K8 protein and the risk of viral hepatatis and acute fulminant hepatatis in human subjects. Establishing the enablement of 2 species (viral hepatatis and AFH) within a genus of thousands of possible species (i.e., any cryptogenic or non-cryptogenic liver disease) is not considered to be sufficient to establish the enablement of a representative number of species within the broadly claimed genus. Applicants response states that the inventors abstract showing the "importance of some K8 variants in African Americans with liver disease" has been submitted to the New England Journal of Medicine. It is acknowledged that Applicants have now submitted a complete copy of the reference to which Applicants previously provided a copy of an abstract. However, this evidence has not been entered and has not been considered because Applicants have not established why this evidence was not earlier presented. Also, as stated in the Office action of January 29, 2009 with respect to the previously filed abstract for this reference, Applicants own reference is not impartial in nature and does not serve as evidence to esablish the enablement of the present invention. MPEP 716.02 states that "The reason for requiring evidence in declaration or affidavit form is to obtain the assurances that any statements or representations made are correct, as provied by 35 U.S.C. 25 and 18 U.S. C. 1001." Permitting a publication to substitute for expert testimony would circumvent the guarantees built into the statute. Ex parte Gray, 10 USPQ2d 1922, 1928 (Bd. Pat. App. & Inter. 1989). Note, that this should not be construed as an invitation for providing additional declarations or affidavits.

In the response, Applicants also state that the objection to the claims should be withdrawn because the claims have been amended so that they are directed to elected Group I. However, claim 1 has not been amended so that it is directed to the elected invention. Group I as set forth in the restiction requirment of March 19, 2008 is limited to methods which detect a predisposition to liver disease by analyzing the genotype of the keratin K8 gene. However, claim 1 encompasses methods which detect mutations in the keratin K18 gene. Further, the invention elected by Applicants was limited to methods which detect the mutation in K8 that encodes the amino acid at position 340. The present claims encompass the detection of additional mutations (i.e., mutations that encode for an amino acid change at position 64-71, 102, 127, 149, 260, 275, 284, 294, 296, and 339 of the K18 protein and mutations that encode for an amino acid change at position 52, 53, 61, 433, 453 and 465-468 of the K8 protein). There are no generic claims on record with respect to the mutations (e.g., claims directed to a method which detects any mutation in K8 nucleic acids) or with respect to the recited genes (i.e., methods which detect a predisposition to a liver disease by detecting a mutation in any gene). As set forth in the restriction requirement of March 19, 2008, upon the allowance of a generic claim, Applicant will be entitled to consideration of claims to additional species. However, since there are no pending claims that are generic to the detection of any K8 mutation and because the subject matter of methods for detecting a predisposition to a liver disease by detecting any K8 mutation has not been found to be allowable, the additionally recited K8 mutations and K18 mutations listed in claim 1 remain withdrawn from consideration.